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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,401	BOZZONI ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/6/2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 18-21 are pending.

Applicant's election without traverse of Group I, claims 18-21 drawn to a nucleic acid encoding a polypeptide having endoribonuclease activity and a vector comprising said nucleic acid, as submitted in a communication filed on 2/15/2007 is acknowledged.

Claims 18-21 are at issue and are being examined herein.

Specification

1. The use of trademarks has been noted in this application. See, for example, "Bluescript" on page 9, line 23, "Centricon" on page 7, line 12, "Vydac" on page 7, line 28, "Procise" on page 7, line 33. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

2. The specification is objected for not complying with sequence rules. Specifically, the term "SEQ ID No X" should be amended to recite " SEQ ID NO: X" throughout the specification. See 37 CFR 1.821. Applicant is requested to make the appropriate changes.

3. The specification is objected to as it lacks a heading indicating where the description of the drawings is in the specification. Appropriate correction is required.

4. The specification is objected to for the following reasons. The sequence listing as filed on 1/6/2005 shows SEQ ID NO: 1 as having 1265 nucleotides and SEQ ID NO: 2 as having 292 amino acids with position 161 being an R (arginine) residue. The specification indicates that Figure 4 shows the cDNA and amino acid sequence of the protein of the invention (XendoU). According to the description

of Figure 4 provided in the specification, the cDNA of XendoU has the sequence set forth in SEQ ID NO: 1 and the amino acid sequence of XendoU is SEQ ID NO: 2. A cursory review of Figure 4 shows that the amino acid sequence of XendoU does not match SEQ ID NO: 2 as provided in the CRF and paper sequence listing because the residue at position 161 in that figure is an E (glutamic acid) residue. Also, a cursory review of Figure 4 shows that the nucleotide sequence of the XendoU cDNA does not match SEQ ID NO: 1 as provided in the CRF and paper sequence listing because the sequence on Figure 4 has 1268 nucleotides. Appropriate correction and/or clarification is required.

Priority

5. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. 119(a)-(d) to ITALY RM2002A000365 filed on 07/08/2002. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

6. This is the US national stage application of PCT/IT03/00424 filed on 07/04/2003.

Information Disclosure Statement

7. The information disclosure statement (IDS) submitted on 1/6/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the Examiner.

Drawings

8. The drawings submitted on 1/6/2005 have been reviewed and are accepted by the Examiner for examination purposes.

Claim Objections

9. Claim 18 is objected to due to the recitation of "ions dependent". It should be amended to recite "ion-dependent". Appropriate correction is required.

10. Claim 18 is objected to due to the recitation of "endoribonucleasic". It should be amended to recite "endoribonuclease". Appropriate correction is required.

11. Claim 19 is objected to due to the recitation of "SEQ ID No 1 nucleotide sequence". The term is redundant as it is understood that SEQ ID No 1 is a sequence. It should be amended to recite "SEQ ID No 1". Appropriate correction is required.

12. Claim 18 is objected to due to the recitation of "single filament specific". While the Examiner has interpreted the term as referring to a single stranded nucleic acid, for consistency with language commonly used in the art, it is suggested the term be amended to recite "single strand specific" or similar. Appropriate correction is required.

13. Claims 20-21 are objected to due to the recitation of "express effectively the inventive nucleic acid in....according to claim 18". For clarity and consistency with commonly used claim language, the term should be amended to recite "express the nucleic acid of claim 18 in....". Appropriate correction is required.

Claim Rejections - 35 USC § 101

14. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

15. Claims 18-19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 18-19, as written, do not sufficiently distinguish over nucleic acids as they exist naturally because the claim(s) does not particularly point out any non-naturally occurring differences between the

claimed product and the naturally occurring product. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claim(s) should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified" as taught by page 9, lines 15-20 of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112, Second Paragraph

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

18. Claim 18 (claims 19-21 dependent thereon) is indefinite in the recitation of "release 2'-3' cyclic phosphate and 5'OH ends cleavage products" because the term is unclear and confusing. As written, the term appears to indicate that as a result of the endoribonuclease acting on a nucleic acid, the products are going to be 2'-3' cyclic phosphate and 5'OH ends. However, it is noted that (1) according to the specification, the product is a nucleic acid which has a 2'-3' cyclic phosphate at the 3' end, and (2) the product of an endoribonuclease acting on a nucleic acid is a fragment of said nucleic acid having a 3' and a 5' end. There is no product which is a 5'OH end. For examination purposes, it will be assumed that the term reads "release cleavage products having a 2'-3' cyclic phosphate at the 3' end. Correction is required.

19. Claim 19 is indefinite in the recitation of "substantially including SEQ ID No 1...functional homologs thereof or a complementary sequence thereto" for the following reasons. First, the term "substantially including" is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of

ordinary skill in the art would not be reasonably apprised of the scope of the invention. In addition, the term "functional homologs" is unclear in view of the fact that the claim is directed to a nucleic acid. Thus, it is unclear if the "function" required in the homolog is that of the protein encoded by the nucleic acid, or if the term refers to an unknown function associated with the nucleic acid itself. The term "complementary sequence" is also indefinite because it is unclear which "complementary sequences" are encompassed by the claim. Fragments of any size which are complementary to the polynucleotide claimed can be considered as being "complementary" to that polynucleotide. Applicants have not define the term "complementary", as it relates to size, in the specification either. In view of the fact that one cannot determine how the claim intends to further limit claim 18, for examination purposes, it will be assumed that claim 19 is a duplicate of claim 18. With regard to the term "complementary", if the intended nucleic acid is the entire complement, the claim should be amended to recite, for example, "completely complementary". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Claims 18-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 18-21 are directed to a genus of nucleic acids encoding proteins which (1) have endoribonuclease activity, (2) are polyU and single strand specific, (3) are Mn^{2+} ion-dependent, and (4)

are able to release cleavage products having a 2'-3' cyclic phosphate at the 3' end. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

There is no structural limitation with regard to the members of the genus of nucleic acids claimed. While the specification in the instant application discloses the structure of a single species of the genus of nucleic acids claimed (i.e., the polynucleotide of SEQ ID NO: 1), it provides no information as to the structural elements required in any nucleic acid encoding a protein having the recited activity, nor does it teach which structural elements within the polypeptide of SEQ ID NO: 2 are required to display the recited functional characteristics. The specification fails to describe any additional species by any relevant, identifying characteristics or properties other than by functionality (i.e., endoribonuclease activity).

The claims encompass a large genus of nucleic acids which are structurally unrelated. A sufficient written description of a genus of nucleic acids may be achieved by a recitation of a representative number of nucleic acids defined by their nucleotide sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. However, in the instant case, there is no structural feature which is representative of all the members of the genus of nucleic acids recited in the claims, and there is no information as to a correlation between structure and function. Furthermore, while one could argue that SEQ ID NO: 2 is representative of the structure of all the members of the genus of proteins encoded by the claimed nucleic acids, such that the recited genus is adequately described by the disclosure of SEQ ID NO: 1-2, it is noted that the art teaches several examples of how even little structural variability can result in major changes in function. For example, Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring *Pseudomonas* enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Therefore, since minor structural changes may result in changes affecting function, and no additional information correlating structure with the recited functional characteristics has been provided, one cannot reasonably conclude that the structures disclosed are representative of all the nucleic acids claimed.

Due to the fact that the specification only discloses a single species of the genus of nucleic acids recited (i.e., SEQ ID NO: 1), as well as the lack of description of any additional species by any relevant, identifying characteristics or properties, one of skill in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention.

22. Claims 18-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid comprising SEQ ID NO: 1 and a vector comprising said nucleic acid, does not reasonably provide enablement for (A) any nucleic acid encoding a protein which (1) has endoribonuclease activity, (2) is polyU and single strand specific, (3) is Mn^{2+} ion-dependent, and (4) is able to release cleavage products having a 2'-3' cyclic phosphate at the 3' end, or (B) vectors comprising the nucleic acids of (A). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows: (1) quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence and absence of working examples, (4) the nature of the invention, (5) the state of prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claims. The factors which have lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed in detail below.

The breath of the claims. Claims 18-21 are so broad as to encompass (1) any nucleic acid encoding a protein which (a) has endoribonuclease activity, (b) is polyU and single strand specific, (c) is Mn^{2+} ion-dependent, and (d) is able to release cleavage products having a 2'-3' cyclic phosphate at the 3' end, and (2) vectors comprising the nucleic acids of (A). See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation. The enablement provided is not commensurate in scope with the claims due to the extremely large number of nucleic acids of unknown structure recited in the claims. In the instant case, the specification enables the polynucleotide of SEQ ID NO: 1.

The amount of direction or guidance presented and the existence of working examples. The specification discloses the amino acid sequence of one protein having the recited endoribonuclease

activity as a working example (SEQ ID NO: 2) and the nucleotide sequence of the corresponding nucleic acid (SEQ ID NO: 1). However, the specification fails to provide any clue as to (1) the structural elements required in any nucleic acid encoding a protein having the recited functional characteristics, or (2) which nucleotides in the polynucleotide of SEQ ID NO:1 can be modified and which ones are to be conserved to create a variant which encodes a protein having the recited activity.

The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art. The nucleotide sequence of the coding region of a polynucleotide encoding a protein determines the structural and functional properties of that protein. In the instant case, neither the specification nor the art provide a correlation between structure and activity such that one of skill in the art can envision the structure of any nucleic acid encoding a polypeptide having the same biological function as that of the polypeptide of SEQ ID NO: 2. In addition, the art does not provide any teaching or guidance as to (1) which nucleotides in the polynucleotide of SEQ ID NO: 1 can be modified and which ones are conserved such that one of skill in the art can make variants as recited encoding polypeptides with the same biological activity as that of the polypeptide of SEQ ID NO: 2, (2) which segments of the polypeptide of SEQ ID NO: 2 are essential for activity, and (3) the general tolerance of endoribonucleases to structural modifications and the extent of such tolerance. The art clearly teaches that changes in a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are required for that activity is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (Introduction to Protein Structure, Garland Publishing Inc., New York, page 247, 1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal

how little is known about the rules of protein stability, and (3) the difficulties in designing *de novo* stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. and Seffernick et al. already discussed above, where it is shown that even small amino acid changes result in enzymatic activity changes.

The quantity of experimentation required to practice the claimed invention based on the teachings of the specification. While methods of generating or isolating variants of a polynucleotide and enzymatic assays were known in the art at the time of the invention, it was not routine in the art to screen by a trial and error process for any number of nucleic acids and determine which ones encode proteins having the recited activity. In the absence of (1) a rational and predictable scheme for determining which nucleic acids are more likely to encode a protein having the desired function, and/or (2) a correlation between structure and activity, one of skill in the art would have to test an essentially infinite number of polynucleotides to determine which ones encode proteins having the recited functional properties. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, as is the case herein, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that a reasonable number of species can be selected for testing. In view of the fact that such guidance has not been provided in the instant specification, it would require undue experimentation to enable the full scope of the claims.

Therefore, taking into consideration the extremely broad scope of the claims, the lack of guidance, the amount of information provided, the lack of knowledge about a correlation between structure and function, the high degree of unpredictability of the prior art in regard to structural changes and their effect on function, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

24. Claims 18-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Laneve et al. (J. Biol. Chem. 278(15):13026-13012, April 2003).

Laneve et al. teach cloning and expression of a protein labeled XendoU from *X. laevis* (Figure 3 discloses the amino acid and cDNA nucleotide sequences), which is characterized as a protein that (1) has endoribonuclease activity, (2) is polyU and single strand specific, (3) is Mn^{2+} ion-dependent, and (4) is able to release cleavage products having a 2'-3' cyclic phosphate at the 3' end (page 13027, left column, lines 1-7). Laneve et al. teach the expression of the XendoU protein in *E. coli* by transforming *E. coli* M15 with a vector encoding a His6-XendoU fusion protein (page 13027, right column, *Isolation of XendoU cDNA and its expression in reticulocyte lysate and in bacteria*).

Claims 18-20 are directed to (A) any nucleic acid encoding a protein that (1) has endoribonuclease activity, (2) is polyU and single strand specific, (3) is Mn^{2+} ion-dependent, and (4) is able to release cleavage products having a 2'-3' cyclic phosphate at the 3' end, and (B) a recombinant vector comprising the nucleic acid of (A) wherein said vector can be expressed in prokaryotic cells. See Claim Rejections under 35 USC 112, second paragraph for claim interpretation. Therefore, the teachings of Laneve et al. anticipate the instant claims as written.

25. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

26. Claims 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Laneve, P. (Purificazione e caratterizzazione di una nuova attivita endoribonucleolitica coinvolta nella biosintesi dei piccolo RNA nucleolari in *X. laevis*, Thesis, 2001; cited in the IDS) as evidenced by GenBank accession number AJ507315 (cited in the IDS).

Claims 18-20 are directed to any nucleic acid encoding a protein that (1) has endoribonuclease activity, (2) is polyU and single strand specific, (3) is Mn^{2+} ion-dependent, and (4) is able to release cleavage products having a 2'-3' cyclic phosphate at the 3' end. See Claim Rejections under 35 USC 112, second paragraph for claim interpretation. GenBank accession number AJ507315 discloses the nucleotide sequence of mRNA encoding a *X. laevis* protein and indicates Laneve, P. as the reference corresponding to the nucleotide sequence disclosed. The mRNA of Laneve, P. (1268 nucleotides long) is identical to the polynucleotide of SEQ ID NO: 1 (1265 nucleotides long) except for 3 contiguous nucleotides which are missing in SEQ ID NO: 1. See alignment provided. These missing nucleotides are not in the coding region of SEQ ID NO: 1, which extends from nucleotides 39-914 according to the sequence listing. Thus, the mRNA of Laneve, P. would encode the same protein of the instant application, which has been disclosed as having the recited functional characteristics. Therefore, the teachings of Laneve, P. anticipate the instant claims as written.

Claim Rejections - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

28. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

29. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Laneve et al. (J. Biol. Chem. 278(15):13026-13012, April 2003). The teachings of Laneve et al. have been discussed above. Laneve et al. do not teach an expression vector which can be used in eukaryotic cells for expression of the XendoU protein.

Claim 21 is directed to a vector comprising the nucleic acid of claim 18 as described above wherein said vector can be used in eukaryotic cells for expression of the endoribonuclease.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an expression vector that can be used in a eukaryotic cell for expression of the XendoU protein of Laneve et al. A person of ordinary skill in the art is motivated to construct such a vector to recombinantly produce the XendoU protein in a system which allows post-translational modifications not provided by a prokaryotic cell, since the XendoU protein is of eukaryotic origin. One of ordinary skill in the art has a reasonable expectation of success at making the vector since construction of expression vectors for eukaryotic systems is well known and widely used in the art. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

30. Claims 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laneve, P. (Purificazione e caratterizzazione di una nuova attivita endoribonucleolitica coinvolta nella biosintesi dei piccolo RNA nucleolari in *X. laevis*, Thesis, 2001; cited in the IDS). The teachings of Laneve, P. have been discussed above. Laneve, P. does not teach an expression vector which can be used in prokaryotic or eukaryotic cells for expression of the *X. laevis* protein.

Claims 20-21 are directed to vectors comprising the nucleic acid of claim 18 as described above wherein said vectors can be used in prokaryotic or eukaryotic cells for expression of the endoribonuclease.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an expression vector comprising the nucleic acid of Laneve, P. that can be expressed in prokaryotic or eukaryotic cells. A person of ordinary skill in the art is motivated to construct such a vector and express the nucleic acid of Laneve, P. for the benefit of recombinantly producing the *X. laevis* protein encoded by said nucleic acid to obtain sufficient amounts of the *X. laevis* protein for further characterization. Recombinant production of proteins is generally considered a preferred method for obtaining a protein since it can potentially produce larger amounts of the product in a consistent fashion, as opposed to isolation from the natural source. In addition, a person of ordinary skill in the art is motivated to construct vectors that can be used in prokaryotic cells because recombinant production of proteins in prokaryotic cells is usually faster, easier and less expensive. A person of ordinary skill in the art is motivated to construct vectors that can be used in eukaryotic cells because prokaryotic cells cannot perform post translational modifications. One of ordinary skill in the art has a reasonable expectation of success at making the vectors because construction of expression vectors to be used in prokaryotic and eukaryotic cells is well known and widely used in the art. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

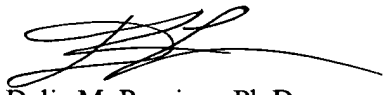
Conclusion

31. No claim is in condition for allowance.

32. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (571) 273-8300. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

33. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



Delia M. Ramirez, Ph.D.
Primary Patent Examiner
Art Unit 1652

DR
March 30, 2007

SEQ ID NO: 1

RESULT 2
XLA507315
LOCUS XLA507315 1268 bp mRNA linear VRT 08-APR-2003
DEFINITION Xenopus laevis mRNA for endoU protein.
ACCESSION AJ507315
VERSION AJ507315.1 GI:22797892
KEYWORDS endoU protein.
SOURCE Xenopus laevis (African clawed frog)
ORGANISM Xenopus laevis
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidea; Pipidae; Xenopodinae; Xenopus; Xenopus.
REFERENCE 1
AUTHORS Laneve,P.
TITLE Purificazione e caratterizzazione di una nuova attivita' endoribonucleolitica coinvolta nella biosintesi dei piccoli RNA nucleolari in X. laevis
JOURNAL Thesis (2001) Department of Genetics and Molecular Biology, University of Rome, Rome, Italy
REFERENCE 2
AUTHORS Laneve,P., Altieri,F., Fiori,M.E., Scaloni,A., Bozzoni,I. and Caffarelli,E.
TITLE Purification, cloning, and characterization of XendoU, a novel endoribonuclease involved in processing of intron-encoded small nucleolar RNAs in Xenopus laevis
JOURNAL J. Biol. Chem. 278 (15), 13026-13032 (2003)
PUBMED 12571235
REFERENCE 3 (bases 1 to 1268)
AUTHORS Caffarelli,E.
TITLE Direct Submission
JOURNAL Submitted (03-SEP-2002) Caffarelli E., Department of Genetics and Molecular Biology, Institute of Molecular Biology and Pathology, University of Rome, P.le Aldo Moro,5, 00185 Rome, ITALY
FEATURES Location/Qualifiers
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CDS 39. .917
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3'UTR 918. .1268
ORIGIN

Query Match 99.0%; Score 1252; DB 11; Length 1268;
Best Local Similarity 99.8%; Pred. No. 0;
Matches 1265; Conservative 0; Mismatches 0; Indels 3; Gaps 1;

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RESULT 3
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ACCESSION   CR942399
VERSION     CR942399.2  GI:77624130
KEYWORDS    .
SOURCE      Xenopus tropicalis (Silurana tropicalis)
  ORGANISM  Xenopus tropicalis
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            Xenopodinae; Xenopus; Silurana.
REFERENCE   1  (bases 1 to 1435)
  AUTHORS   Amaya,E., Ashurst,J.L., Bonfield,J.K., Croning,M.D.R., Chen,C.-K.,
            Davies,R.M., Francis,M.D., Garrett,N., Gilchrist,M.J.,
            Grafham,D.V., McLaren,S.R., Papalopulu,N., Rogers,J., Smith,J.C.,
            Taylor,R.G., Voigt,J. and Zorn,A.M.
  TITLE     Direct Submission
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